Author's response to reviews

Title: Depression Treatment Patterns Among Individuals with Osteoarthritis: A Cross Sectional Study

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Author's response to reviews: see over
Dear Editor,

Thank you for considering our revised manuscript entitled, “Depression treatment patterns among individuals with arthritis: A cross sectional analysis”. We appreciate the reviewer’s comments and feedback. Please find below point-by-point response to reviewer’s comments and the changes that we have made in the manuscript.

**Reviewer 1 & Reviewer 2**

1. The pathogenesis, clinical manifestations, associated risk factors and treatment is completely difference between RA and OA. Grouping RA and OA together to do the analyses are not helpful. Is it possible to look at RA and OA separately? Also, there is no information of how many arthritis patients was suffering from secondary fibromyalgia that is more associated with depressive symptoms rather than disease activity itself.

2. I am concerned that patients with RA and OA were combined. The authors state that they combined RA and OA into one group because of “their biological link with depression.” However these are two very different conditions (one is a pro-inflammatory autoimmune disease and the other is a consequence of mechanical wear-and-tear) with different prevalence’s of depression, different pathophysiology, and different mechanisms for depression. The authors need to compare the patients with OA and RA to see if these groups can be combined. I imagine that patients with OA far outnumber patients with RA and if the groups are not similar then perhaps patients with RA should be excluded?

As per the reviewers’ recommendations we compared the patients with Rheumatoid arthritis (RA) and Osteoarthritis (OA) and found that patients with OA outnumbered the patients with RA. We also compared individuals with OA and RA and found these two groups were significantly different by age, race/ethnicity, education, poverty status, mental and physical health status (p < .05). Therefore, as per the reviewer’s recommendation we excluded individuals with RA from our study sample.

To be consistent with this change, we have also revised the title of the paper. The title now reads “Depression Treatment Patterns among Individuals with Osteoarthritis: A Cross Sectional Study.”

In addition, we updated data as newer data became available. The current study now includes data from 2008 and the most recent available annual release of MEPS, 2010.

**Major Compulsory Revisions**

1. It seems that patients were included if they had one ICD-9 code for RA or OA but subjects should have had at least 2 face-to-face physician encounters with different dates of service during the measurement time-frame for a diagnosis of RA/OA. This is due to the fact patients may be seen for a one-time “rule-out visit.” A visit may be coded at one visit for arthritis but the patient does not actually have the diagnosis. Two visits coded for the RA or OA gets around this problem. Here is the reference: Gabriel et al. The sensitivity and specificity of computerized databases for the diagnosis of rheumatoid arthritis. Arthritis Rheum. 1994 Jun;37(6):821-3. PMID: 8003054

We appreciate the reviewers’ comment about the number of physician encounters with different dates of services to extract clinical diagnosis of RA and OA. As per the reviewer’s suggestion we analyzed the number outpatient visits for individuals with OA and found that the mean number of outpatient visits per individual was 16 with standard deviation of 0.64. It has to be noted that arthritis is a priority condition in the Medical Expenditure Panel Survey (MEPS). Therefore, detailed probes and queries were conducted to capture information on diagnosed Arthritis. Furthermore,
information in the household component of MEPS has been compared with provider reported data and it has been found to be reliable in published literature (1). MEPS is a reliable population-based database and numerous studies have been published using MEPS (2). It has also been used by public health agencies in US to estimate prevalence of arthritis and associated healthcare expenditures (3).

2. **Table 1 should be patient characteristics organized by the outcome not by different conditions. In other words there should be 3 columns - Column 1 – all arthritis patients, Column 2 - arthritis patients with antidepressant use, Column 3 - Arthritis patients with antidepressant use + psychotherapy. The point of the paper is to see differences by prescription patterns not differences among chronic conditions.**

As suggested by reviewer 1, we have now revised Table 1; it now presents patient characteristics depression treatment groups among individuals with OA.

**Minor essential revisions**

1. **The authors state that depression can cause pain but this relationship is bi-directional. (1st paragraph page 3, 1st paragraph page 8) and the authors need to better clarify the complicated relationship between pain and depression. Pain can lead to depression as well. The authors indirectly show this when they discuss that treatment of pain can improve depressive symptoms in the next paragraph.**

We acknowledge that the relationship between pain and depression is bi-directional, although we cannot measure the bi-directional relationship with a cross-sectional study design. However, to address the concern of the reviewer, we have added new text on page 3 (Background – paragraph 1) and supported it with published research.

We have added the following new text in the manuscript -

“Similarly, pain can also lead to depression, suggesting that the relationship between depression and pain is bi-directional (9). Therefore, the management strategies for depression need to take into account both depressive symptoms and pain (10).”

2. **Disability/Poor function is strongly associated with depression in patients with arthritis and is a potential confounder. The authors need to control for poor function and if there was no measure of disability in the data then this should be mentioned in the limitations section.**

We agree with the reviewer that disability/poor function can be strongly associated with depression in individuals with arthritis. However, in our study sample, functional status was not associated with depression treatment once we controlled for physical and mental health status.

3. **The statistical methods used should be described better. Were the covariates normally distributed? Were the data examined for interactions, effect modifiers?**

As our statistical model was based on a theoretical framework specified on page 4 of the manuscript, we did not examine any interactions or effect modifiers. The current study focuses on the direct cross-sectional associations between patient characteristics and depression treatment. We used standard statistical techniques such as chi-square and multinomial logistic regression, which are commonly used to analyze factors associated with categorical dependent variables.

**Reviewer 2**
Major Compulsory Revisions

3. All the patients included in this survey had depressive disorders (presumably symptomatic and got referred to the psychiatrists) and therefore more than 59% of patients required medication treatment. What can be derived from the results is perhaps the “severity” of depressive disorders in RA/OA is no different from other conditions so that the need for drug treatment is the same. There is no information on the true incidence of depressive disorders (symptomatic) among patients with OA/RA as compared to other chronic joint conditions or illnesses. Moreover, in the discussion part, there are no postulations to explain why in model 4, after adding covariates related to transportation to clinic (metro status), the statistical significance is lost. Does this mean patients with RA/OA had more difficulty in attending clinics (because of arthritis) and they were less likely to accept medication treatment or more frequent follow-up? The authors may need to elaborate in the Discussion on the interpretation of their results eg. Factors related to the increase in the need for anti-depressive treatment in RA/OA but somehow statistically, the difference is not significant, and the possible explanation for this.

As per reviewer 1 and 2 we excluded individuals with RA from our grouping of chronic conditions and reanalyzed the data with same model specifications as in the original version. In these analyses we did not find a statistically significant association between type of chronic condition and depression treatment. Results are summarized in Appendix A.

As suggested by reviewer 1, we have eliminated the comparative analysis of depression treatment among chronic conditions.

Regarding the comment on metro status, we do note that this point is no longer relevant, as our comparative analysis indicated no changes in the association between type of chronic condition and depression treatment across different models. (Please see Appendix A).

4. Regarding disease controls, how about those patients with chronic pain due to neuropathy / neuralgia? Why were these patients not included from the database for comparison?

We recognize the importance of including chronic pain due to neuropathy in our analysis. However, as suggested by reviewer 1 and to substantially shorten the article, we have narrowed the focus to analyzing depression treatment patterns among those with OA. Furthermore, we used pain as an indicator variable (pain arising from any chronic condition) in our multivariable models.

5. The article is unduly long and difficult to understand. It has to be substantially shortened.

We have substantially shortened the article. Eliminating comparative analysis of depression treatment by type of chronic conditions (as suggested by reviewer 1) enabled us to reduce the length of the manuscript. All the text and tables are revised to reflect this change.

EDITORS REQUEST

1. Acknowledgement/ Copyediting

Our manuscript was reviewed by a fluent English speaking colleague, Ms. Kathryn Flack. We have acknowledged her contribution.
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2. **Data availability**

We have documented in the methods section of the manuscript that the dataset is available for public use (Data source-page 5-paragraph 1) and can be directly downloaded by the researchers from http://meps.ahrq.gov/mepsweb/.

**References**


### Appendix A

**Odds Ratios and Adjusted Odds Ratios and 95% Confidence Intervals of Type of Chronic Condition from Multinomial Logistic Regressions on Depression Treatment Among Individuals with Depression**

**Medical Expenditure Panel Survey, 2006 and 2008**

<table>
<thead>
<tr>
<th></th>
<th>Antidepressants Only</th>
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<th>Psychotherapy and Antidepressants</th>
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<tr>
<td></td>
<td>OR</td>
<td>95% CI</td>
<td>sig</td>
<td>OR</td>
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<tr>
<td><strong>MODEL 1</strong></td>
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<tr>
<td>Osteoarthritis</td>
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<td>[0.84,1.94]</td>
<td>1.39 [0.86,2.24]</td>
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<td>Other Joint Disorders</td>
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<td>[0.73,1.44]</td>
<td>0.99 [0.64,1.52]</td>
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<td><em>Other Chronic Conditions (Reference Group)</em></td>
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<td></td>
<td></td>
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<td></td>
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<tr>
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<td>95% CI</td>
<td>Sig</td>
<td>AOR</td>
</tr>
<tr>
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<td>[0.85,1.97]</td>
<td>1.37 [0.85,2.21]</td>
<td></td>
</tr>
<tr>
<td>Other Joint Disorders</td>
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<td><em>Other Chronic Conditions (Reference Group)</em></td>
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<td>0.97 [0.62,1.51]</td>
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<td>0.98 [0.63,1.54]</td>
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<tr>
<td><em>Other Chronic Conditions (Reference Group)</em></td>
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</tbody>
</table>

Note: Based on adults who were alive during the calendar years, aged 21 years older, with self-reported depression and having any one of the following conditions: Osteoarthritis, other joint disorders, chronic obstructive pulmonary disease, diabetes, heart disease, and stroke.

Asterisks represent significant group differences by type of chronic conditions compared to the reference group from multinomial logistic regressions. Model 1 included only type of chronic conditions and predisposing factors. Model 2 included type of chronic conditions, predisposing and enabling factors. Model 3 included type of chronic conditions, predisposing, enabling and need factors. Model 4 included type of chronic conditions, predisposing, enabling,need factors, personal health practices and external healthcare environment. The reference group for the dependent variable in the multinomial logistic regressions was "No Depression Treatment".

AOR: Adjusted odds ratio; CI: Confidence Interval; Sig: significance.

*** p< .001; ** .001 ≤ p < .01; * .01 ≤ p < .05